REMARKS

1. Formal Matters

Claims 17-36 are pending in this application. Claims 17-24, 31 and 32 are amended; claims 25-30 and 33-36 are hereby canceled without prejudice to pursuing claims with similar scope in a continuing application; and claims 37-42 are new. Upon entry of these amendments, claims 17-24, 31, 32, and 37-42 are pending and under active consideration. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the instant application.

2. Amendments to the Claims

Claim 17 is amended to recite that the nucleic acid consists of X nucleotides wherein X = 18 to 120, which is a rephrasing of the limitation of previously-presented claim 17 that the nucleic acid consists of 18 to 120 nucleotides. This claim is also amended to recite that the sequence of the nucleic acid comprises at least Y consecutive nucleotides of SEQ ID NO: 8797, wherein $Y \geq 18$, and wherein $X \geq Y$. These limitations rephrase the stamement "the sequence comprises at least 18 consecutive nucleotides of SEQ ID NO: 8797" in previously presented claim 17. These amendments do not change the scope of the claim.

Claim 18 is amended to recite that the Y nucleotides of the nucleic acid are of SEQ ID NOs: 5135 or 6033, which is a rephrasing of the limitation "the at least 18 nucleotides is of a sequence selected from the group consisting of SEQ ID NOs: 5135 or 6033" in previously presented claim 18. Antecedent basis for Y nucleotides can be found in amended claim 17.

Claim 19 is amended to recite that the Y nucleotides of the nucleic acid are of SEQ ID NOs: 5136 or 6034, which is a rephrasing of the limitation "the at least 18 nucleotides is of a sequence selected from the group consisting of SEQ ID NOs: 5136 or 6034" in previously presented claim 19. Antecedent basis for Y nucleotides can be found in amended claim 17.

Claim 20 is amended to recite that the nucleic acid has a length wherein X = 18 to 24, which is a rephrasing of the limitation "the nucleic acid consists of 18 to 24 nucleotides" in previously presented claim 20. Antecedent basis for Y nucleotides can be found in amended claim 17.

Claim 21 is amended to recite that the nucleic acid has a length wherein X = Y, thereby directing this claim to a nucleic consisting of at least 18 consecutive nucleotides of SEQ ID NO: 8797, an RNA equivalent thereof, or the complement thereof. Support for amended claim 21 can be found in previously presented claim 17 at SEQ ID NO: 8797 of the instant sequence listing, and paragraph 0013 of the application as originally filed, which discloses that the nucleic acids of the instant application may be 18 to 24 nucleotides in length. Antecedent basis for X and Y can be found in amended claim 17.

Claim 22 is amended to recite the nucleic acid of claim 18, wherein X = Y, which is a rephrasing of the limitation "the at least 18 nucleotides is of a sequence of SEQ ID NOs: 5135 or 6033" in previously presented claim 22. Antecedent basis for X and Y can be found in amended claim 17.

Claim 23 is amended to recite the nucleic acid of claim 19, wherein X = Y, which is a rephrasing of the limitation "the at least 18 nucleotides is of a sequence of SEQ ID NOs: 5136 or 6034" in previously presented claim 23. Antecedent basis can be found in amended claim 17.

Claim 24 is amended to recite the nucleic acid of claim 20, wherein X = Y, which is a rephrasing of the limitation of previously-presented claim 24 that the nucleic acid consists of 18 to 24 nucleotides, and which has antecedent basis in amended claim 17.

Claim 31 is amended to recite that the vector comprises the nucleic acid of claim 17, which is a rephrasing of the limitation of previously-presented claim 31 that the vector comprises an insert, wherein the insert consists of the nucleic acid of claim 17.

Claim 32 is amended to recite that the vector comprises the nucleic acid of claim 18, which is a rephrasing of the limitation of previously-presented claim 32 that the vector comprises an insert, wherein the insert consists of the nucleic acid of claim 18. Applicant submits that the specified amendments to claims 18-20, 22-24, 30, and 31 are for reasons of clarification, and not for reasons of patentability.

New claims 37 through 42 recite vectors comprising the nucleic acid of claims 19 through 24, respectively, support for which can be found at paragraph 0022 of the application as originally filed and as described above for amended claims 19 through 24.

3. Patentability Remarks

a. 35 U.S.C. § 112, second paragraph

On page 3 of the Office Action, the Examiner rejects claims 17-36 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner alleges that the term "at least 60/85" in claim 17 and the term "at least 12/22" in claims 29 and 30 are unclear. The Examiner also asserts that the term "system" in claims 35 and 36 is vague and unclear. Finally, the Examiner asserts that claim 21 is not further limiting of claim 17, and claims 22/23 are not further limiting of claims 18/19. The Applicant respectfully disagrees.

In order to expedite prosecution, and without prejudice to seeking similar claims in a continuing application, Applicant has removed the phrase "sequences at least 60/85 to Y consecutive nucleotides of SEQ ID NO. 8797" from claim 17, and canceled claims 29, 30, 35, and 36 without prejudice, thereby rendering the above-specified indefiniteness issues to these claims moot.

With regard to the Examiner's assertion that claim 21 is not further limiting of claim 17, the Applicant respectfully submits that claim 17 is directed to the nucleic acid of 18 to 120 nucleotides comprising at least 18 consecutive nucleotides of SEQ ID NO: 8797. Accordingly, the nucleic acid of

claim 17 may include sequences other than those of SEQ ID NO: 8797. In contrast, amended claim 21 is directed to a nucleic acid that consists of at least 18 nucleotides of SEQ ID NO: 8797. The nucleic acid of claim 21 may only include the sequence of SEQ ID NO: 8787 and no other sequences. Accordingly, claim 21 is further limiting of claim 17.

With regard to the Examiner's assertion that claims 22 and 23 are not further limiting from claims 18 and 19, Applicant respectfully submits that similar to claim language of amended claims 17 and 21 as described above, the nucleic acids of amended claims 18 and 19 may comprise or include sequences other than at least 18 consecutive nucleotides of SEQ ID NOs: 5135 or 6033, or SEQ ID NOs: 5136 or 6034, respectively. In contrast, the nucleic acids of claims 22 and 23 consist or must be at least 18 consecutive nucleotides of SEQ ID NOs: 5135 or 6033, or SEQ ID NOs: 5136 or 6034, respectively. Accordingly, no additional sequences are encompassed by amended claims 22 and 23. In view of the foregoing amendments and remarks, Applicant respectfully requests that the rejection of claims 17-36 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite, be reconsidered and subsequently withdrawn.

b. 35 U.S.C. § 112, first paragraph

On page 4 of the Office Action, the Examiner rejects claims 17-36 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserts that no support has been found in the specification for the ratio "60/85" recited in claims 17 and 20. The Examiner also asserts that no support has been found in the specification for the ratio "12/22" recited in claims 29 and 30. On pages 4 and 5 of the Office Action, the Examiner further asserts that the specification and claims do not adequately describe the genus comprising polynucleotides with variable sequences within SEQ ID NOs: 8797, 5135, 5136, 6033, or 6034, nor the genus comprising these polynucleotides that are at least 12/22 complementary to any binding site sequence of a target gene. Finally, the Examiner further asserts that no support has been found in the specification for the size limitations of 18-120 or 18-24 nucleotides, which are recited in claims 17-20. The Applicant respectfully disagrees.

As discussed above, the Applicant has removed the phrase "sequences at least 60/85 to Y consecutive nucleotides of SEQ ID NO. 8797" from claim 17, and canceled claims 25-30 and 33-36 without prejudice. Accordingly, the objections to the ratio variants of claims 17, 20, 29, and 30 are moot.

With regard to the Examiner assertion that there is no support in the specification for the size limitations of 18-24 or 18-120 nucleotides, Applicant respectfully submits that paragraph 0013 of the specification as filed discloses nucleic acids with lengths ranging from 18 to 120 nucleotides. Accordingly, the specification provides the suitable length limitations for the claimed nucleic acids. In view of the foregoing amendment and remarks, the Applicant respectfully requests that the rejection of

claims 17-36 under 35 U.S.C. §112, first paragraph, for allegedly lacking written descriptive support, be reconsidered and subsequently withdrawn.

c. 35 U.S.C. § 101

On pages 5-7 of the Office Action, the Examiner rejects claims 17-36 under 35 U.S.C. §101, for allegedly lacking utility. In order to satisfy the utility requirement under the Revised Interim Utility Guidelines, a specific and substantial utility must either (i) be cited in the specification or (ii) be recognized as well established in the art, and the utility must be credible.

(1) Specific Utility

A specific utility is defined in the Revised Interim Utility Guidelines Training Materials ("RIUGTM") as a utility that is specific to the particular claimed subject matter, which is in contrast to a general utility that would be applicable to a broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" is not considered to be specific **in the absence of a disclosure of a specific DNA target**. *See* RIUGTM at page 5.

At page 7 of the Office Action, the Examiner alleges that the specification does not disclose any property or activity for the claimed polynucleotides. Applicant respectfully disagrees. The specification identifies **specific** genes of interest that the claimed polynucleotides may be used to regulate expression.

At paragraphs 4799 and 4800 of the specification, it is asserted that the disclosed polynucleotides may be used to target and modulate expression of particular mRNA transcripts. Furthermore, paragraphs 4792, 4793, and 4805 of the specification disclose that the claimed polynucleotides, which are related to the miRNA encoded by the GAM334 gene, modulate expression of particular target mRNA transcripts as shown in Table 2. Table 2 discloses that B3GALT2, CEP1, FKRP, GAB2, HYAL3, IHPK3, MECP2, and ZIC1 are specific target genes for the miRNA related to the claimed polynucleotides.

Similarly, paragraphs 5639 and 5640 of the specification assert that the disclosed polynucleotides may be used to target and modulate expression of particular mRNA transcripts. Furthermore, paragraphs 5632, 5633, and 5645 of the specification disclose that the claimed polynucleotides, which are related to the miRNA encoded by the GAM390 gene, modulate expression of particular target mRNA transcripts as shown in Table 2. Table 2 discloses that APOBEC2, HR, KCNK7, MYLK, PLA2G10, PTPRN, REV3L, SLC9A1, and TAF56 are specific target genes for the miRNA related to the claimed polynucleotides. Accordingly, Applicant respectfully submits that the specification provides a specific utility for the claimed polynucleotides.

(2) Substantial Utility

A substantial utility is defined in the RIUGTM as a utility that defines a "real world" use, which is in contrast to the need to carry out further research to identify or confirm a "real world" context. As discussed above, the claimed polynucleotides may be used to regulate expression of proteins encoded by the B3GALT2, CEP1, FKRP, GAB2, HYAL3, IHPK3, MECP2 and ZIC1 genes. Brockington *et al., Am. J. Hum. Genet.* 69:1198-1209 (Epub, Oct., 2001), which is submitted on the Information Disclosure Statement filed herewith, discloses that the gene FKRP (Fukutin-Related Protein) is known to be associated with the disease congenital muscular dystrophy. The claimed GAM390 polynucleotide may be used to regulate expression of proteins encoded by the APOBEC2, HR, KCNK7, MYLK, PLA2G10, PTPRN, REV3L, SLC9A1, and TAF56 target genes. Sprecher *et al., Am. J. Human Genet.* 64:1323-1329 (1999), which is submitted on the Information Disclosure Statement filed herewith, discloses that the gene HR (hairless protein) is known to be associated with the disease atrichia with papular lesions (APL). One of ordinary skill in the art would recognize that the claimed polynucleotide may be used to regulate expression of genes of interest such as FKRP and HR. Accordingly, Applicant respectfully submits that the specification provides a substantial utility for the claimed polynucleotides.

(3) Credible Utility

According to the RIUGTM, an asserted utility is credible if the assertion is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided. An assertion is credible unless (i) the logic underlying the assertion is **seriously flawed**, or (ii) the facts upon which the assertion is based are **inconsistent** with the logic underlying the assertion. *See* RIUGTM at page 5.

At page 7 of the Office Action, the Examiner asserts that a credible utility is lacking because the claimed polynucleotides are derived from a conceptual model and have not been identified in any biological systems. Applicant respectfully disagrees. Applicant respectfully submits that the Examiner has not considered the asserted utility as discussed above for using the claimed polynucleotides for modulating expression of specific mRNA targets. Whether or not the claimed polynucleotides actually exist in a biological system is irrelevant. The proper inquiry is instead whether a person of ordinary skill in the art would believe that the claimed polynucleotides may be used to modulate expression of the specific mRNA targets.

Paragraph 0097 of the application discloses that the mRNA targets of the claimed polynucleotides were identified as being consistent with the 2D structures and free-energy of target binding site to known miRNAs. The method as described in paragraph 0097 for identifying target binding sites of miRs is based upon studies at the time of filing demonstrating miRs binding to target binding sites as disclosed in references such as Wightman et al., 1993, Reinhart et al., 2000, Slack et al. 2000, and Moss et al., 1997, which are all cited in the Information Disclosure Statement filed October 26, 2006 under reference

numbers 10, 260, 300, and 100 respectively. In view of the asserted utilities being consistent with the general understanding of miRNAs and target binding sites at the time of filing, Applicant's respectfully submit that one of ordinary skill in the art would believe that each of the claimed polynucleotides would bind their respective target binding sites.

In view of the foregoing remarks and lack of a showing that the assertion is seriously flawed or logically inconsistent, the Applicant respectfully submits that a credible utility is asserted for the claimed polynucleotides.

(4) Conclusion

In summary, the Applicant submits that the specification asserts that the claimed polynucleotides may be used to modulate expression of specific target genes linked to particular diseases of interest, and that one of ordinary skill in the art would believe the assertion. In view of the foregoing remarks, the Applicant respectfully request that the rejection of claims 17-34 under 35 U.S.C. §101 be reconsidered and subsequently withdrawn.

d. 35 U.S.C. § 102(a), claims 17, 18, 20-22, 24, and 31-34 over Gunderson

On page 8 of the Office Action, the Examiner rejects claims 17, 18, 20-22, 24, and 31-34 under 35 U.S.C. § 102(a) as allegedly being anticipated by Gunderson (WO 200216649). The Examiner asserts that Gunderson teaches an isolated nucleic acid consisting of 18-24 nucleotides comprising or consisting of at least 18 consecutive nucleotides that share at least 70% identity with SEQ ID NO: 6033, or the complement thereof. Applicant respectfully disagrees in view of the foregoing amendments.

Specifically, amended claim 17 is directed to an nucleic acid that comprises at least 18 consecutive nucleotides of SEQ ID NO: 8797, therefore requiring 100% identity to a sequence of SEQ ID NO: 8797. Gunderson does not teach a nucleic acid meeting this structural limitation, because the nucleic acid of Gunderson is only 73.7% identical to the claimed nucleic acids. Accordingly, Gunderson does not anticipate the nucleic acid of amended claim 17. As discussed above, dependent claims 18, 20-22, 24, 31, and 32 have the same limitations of amended claim 17 and claims 33 and 34 have been canceled without prejudice. In view of the foregoing amendments and remarks, Applicant respectfully requests that the rejection of claims 17, 18, 20-22, 24, and 31-34 under 35 U.S.C. § 102(a) over Gunderson be reconsidered and withdrawn.

e. 35 U.S.C. § 102(b), claims 17, 19-21, 23, 24, 31, 33, and 34 over Allawi

On pages 8-9 of the Office Action, the Examiner rejects claims 17, 19-21, 23, 24, 31, 33, and 34 under 35 U.S.C. § 102(b) as allegedly being anticipated by Allawi et al. (WO 20019037). The Examiner asserts that Allawi teaches an isolated nucleic acid consisting of 18-24 nucleotides comprising or consisting of at least 18 consecutive nucleotides that share at least 70% identity with SEQ ID NO: 5136.

Applicant respectfully disagrees in view of the foregoing amendment. As described above, amended claim 17 is directed to a nucleic acid comprising at least 18 consecutive nucleotides of SEQ ID NO: 8797. Allawi does not teach a nucleic acid meeting this structural limitation. Rather the nucleic acid of Allawi is only 70% identical to the claimed nucleic acids. In view of the foregoing amendments and remarks, Applicant respectfully requests that the rejection of 17, and its dependent claims 19-21, 23, 24, 31, 33, and 34 under 35 U.S.C. § 102(b) over Allawi be reconsidered and withdrawn.

f. 35 U.S.C. § 102(a), claims 17, 19-21, 23, 24, and 31-34 over Gunderson

On page 9 of the Office Action, the examiner rejects claims 17, 19-21, 23, 24, and 31-34 as allegedly being anticipated by Gunderson. The Examiner asserts that Gunderson teaches an isolated nucleic acid consisting of 18-24 nucleotides comprising or consisting of at least 18 consecutive nucleotides that share at least 70% identity with SEQ ID NO: 6034. Applicant respectfully disagrees in view of the foregoing amendment.

Amended claim 17 is directed to a nucleic acid comprising at least 18 consecutive nucleotides of SEQ ID NO: 8797. Gunderson does not teach a nucleic acid that is 100% identical to at least 18 consecutive nucleotides of SEQ ID NO: 8797. As described above, the nucleic acid of Gunderson is only 73.7% identical to the claimed nucleic acids. In view of the foregoing amendments and remarks, Applicant respectfully requests that the rejection of claims 17, 19-21, 23, 24, and 31-34 under 35 U.S.C. § 102(a) over Gunderson be reconsidered and withdrawn.

4. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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